Indian Institute of Science
Centre for BioSystems Science and Engineering

BSSE Colloquium

7 October 2020, 04:00 PM, Virtual

Investigation of cell membrane dynamics: A potential marker for lipid response towards membrane-active

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ABSTRACT:

The cell membrane is made up of lipids and proteins held together by intermolecular hydrophobic/hydrophilic interactions. Binding of membrane targeting molecules to the lipid bilayer is an important step that occurs when pathogens infect host cells as well as when antibiotics are targeted against pathogens. Unravelling the underlying physical interactions between membrane targeting molecules of both prokaryotic and eukaryotic cell membranes is crucial to developing strategies to mitigate virulent diseases. In this colloquium, I will emphasize the importance of understanding the dynamics of membrane lipids which serve as unique markers to identify and characterize protein/peptide-lipid interactions when membrane targeting molecules associate with cell membranes.

During the first part of the talk, I will discuss our results on the interaction of the pore-forming toxin, listeriolysin O (LLO) used by the bacteria Listeria monocytogenes to attack and disrupt the host cellular machinery. LLO oligomerizes upon binding to the lipid bilayer forming either complete rings or incomplete arcs that are observed to exist in a membrane inserted pore state or as uninserted pre-pore state. Using Förster resonance energy transfer (FRET) and confocal fluorescence correlation spectroscopy (FCS), the significant outcome from this part of the study is our ability to identify distinct signatures of various structural states of LLO and their influence on modulating lipid dynamics.

For a deeper understanding of the connection between membrane bound LLO oligomers (arcs and rings) on lipid dynamics, the results from a concentration-dependent study to correlate oligomeric states with the lipid dynamics will be discussed in the second part of my talk. The lipid dynamics undergo a dynamical cross-over, correlated with transitions of LLO oligomeric state populations from rings to arc-like pore complexes. The proposed two-state free area-based diffusion model predicts oligomeric state populations of LLO, illustrating the link between lipid loss and crowding induced changes upon pore formation.

In the last part of the talk, I will shift focus to understand lipid response from the pathogens' point of view. Targeting bacterial cell membranes become essential in our quest for antimicrobial molecules to combat pathogens in this emerging antibiotic-resistant era. In this part of the study, we tracked the lipid mobility in live bacterial cell envelopes and observed significant changes to the lipid mobility in the presence of membrane targeting antibiotics. Interestingly, we could correlate this change in lipid mobility as a signature of antibiotic action rather than a consequence of a stress-induced physical response of the cell.

To conclude, variations in the lipid mobility provides a unique fingerprint to monitor changes that occur in the cell membrane. Our findings reveal the intimate connection between lipid dynamics and the different oligomeric states of proteins or antibiotics that associate with the membrane. Our study has broad implications in membrane repair processes providing novel molecular insights to mitigate bacterial virulence by compromising the action of pore forming toxins or developing suitable target molecules to disrupt the bacterial cell wall.